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## Review

## The use of non-invasive ventilation in COVID-19: A systematic review



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## ABSTRACT

**Objective:** Guidelines from different regions on the use of non-invasive ventilation in COVID-19 have generally been inconsistent. The aim of this systematic review was to appraise the quality and availability of guidelines, and whether non-invasive ventilation in the early stages of the pandemic is of importance. **Design and method:** Databases, including PubMed, Web of Science, and Cochrane Library, as well as

**Abbreviations:** AGREE, Appraisal of Guidelines for Research and Evaluation; BiPAP, bilevel positive airway pressure; COVID-19, coronavirus disease 2019; CPAP, continuous positive airway pressure; FiO<sub>2</sub>, fraction of inspired oxygen; GRADE, Grading of Recommendations Assessment, Development and Evaluation; ICC, intraclass correlation coefficient; ICU, intensive care unit; NI-CPAP, non-invasive continuous positive airway pressure; NIPPV, nasal intermittent positive pressure ventilation; NIV, non-invasive ventilation; PaCO<sub>2</sub>, partial pressure of carbon dioxide in artery; PEEP, positive end-expiratory pressure; PPE, personal protective equipment; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; SpO<sub>2</sub>, peripheral oxygen saturation; ARIR & AIFI, Italian Association of Respiratory Physiotherapists & Italian Association of Physiotherapists, Respiratory physiotherapy in patients with COVID-19 infection in acute setting: a position paper of the Italian Association of Respiratory Physiotherapists; ASID, Australasian Society for Infectious Diseases, Interim guidelines for the clinical management of COVID-19 in adults; BTS, British Thoracic Society, Use of acute NIV in patients hospitalized with suspected or confirmed COVID-19 infection; BTS (guidance), British Thoracic Society, Respiratory support of patients on medical wards; CCCGWG, COVID-19 Clinical Care Guidance Working Group, Clinical management of patients with moderate to severe COVID-19 – interim guidance; CTS & CACP, Chinese Thoracic Society & Chinese Association of Chest Physicians, Guidance for the management of adult patients with coronavirus disease 2019; ICSI, Intensive Care Society of Ireland, Guidance document for the intensive care management of the adult patient with confirmed or suspected COVID-19; Indian CDC, Indian Centers for Disease Control and Prevention, Guidelines on clinical management of severe acute respiratory illness (SARI) in suspect/confirmed novel coronavirus (nCoV) cases; INMI, National Institute for Infectious Diseases, National Institute for the Infectious Diseases “L. Spallanzani”, IRCCS, Recommendations for COVID-19 clinical management; ITS & IRS, Italian Thoracic Society & Italian Respiratory Society, Managing the respiratory care of patients with COVID-19; NCCET, National COVID-19 Clinical Evidence Taskforce, Australian guidelines for the clinical care of people with COVID-19; NHC & SATCM, National Health Commission & State Administration of Traditional Chinese Medicine, Diagnosis and treatment protocol for novel coronavirus pneumonia (Trial version 7); NHS (critical care), National Health Service, Clinical guide for the management of critical care for adults with COVID-19 during the coronavirus pandemic; NHS (NIV), National Health Service, Guidance for the role and use of non-invasive respiratory support in adult patients with COVID-19 (confirmed or suspected); NHS (management), National Health Service, Clinical management of persons admitted to hospital with suspected COVID-19 infection; NIH, National Institutes of Health, Coronavirus disease 2019 (COVID-19) treatment guidelines; PAHO, Pan American Health Organization, Guidelines for critical care of seriously ill adult patients with coronavirus (COVID-19) in the Americas; PCS, Pakistan Chest Society, COVID-19 management guidelines; SIAARTI & EAMS, Società Italiana di Anestesia Analgesia Rianimazione e Terapia Intensiva & European Airway Management Society, The Italian coronavirus disease 2019 outbreak: recommendations from clinical practice; SIMIT, Lombardy Section of the Italian Society of Infectious and Tropical Diseases, Guidelines for the treatment of people with COVID-19 disease, edition 2.0, 13 March 2020; SSC, Surviving Sepsis Campaign, Guidelines on the management of critically ill adults with coronavirus disease 2019 (COVID-19); SSIICM, Swiss Society of Intensive Care Medicine, Recommendations for the admission of patients with COVID-19 to intensive care and intermediate care units (ICUs and IMCUs); Kluge et al., German recommendations for critically ill patients with COVID-19; Thomas et al., Physiotherapy management for COVID-19 in the acute hospital setting: recommendations to guide clinical practice; WHO, World Health Organization, Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected: interim guidance v. 1.2; WHO-toolkit, World Health Organization, Clinical care for severe acute respiratory infection: toolkit – COVID-19 adaptation.

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**Keywords:**

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 Non-invasive ventilation  
 Respiratory failure  
 Guidelines  
 AGREE II

websites of international organizations and gray literature, were searched up to June 23, 2020. The reference lists of eligible papers were also hand-searched.

**Results:** A total of 26 guidelines met the inclusion criteria. According to the Appraisal of Guidelines for Research and Evaluation (AGREE) II instrument, the guidelines' methodological quality was low. Among six domains, *Rigour of Development* and *Editorial Independence* were of the lowest quality. Given the lack of evidence from randomized clinical trials and the great variation between different regions, recommendations for non-invasive ventilation have generated considerable debate regarding the early stages of COVID-19.

**Conclusions:** Improving the methodological quality of the guidelines should be a goal with regard to future pandemics. Additionally, better-designed randomized clinical trials are needed to resolve contradictions regarding the impact of non-invasive ventilation.

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## Introduction

The outbreak of COVID-19 began in Wuhan, China, in late December 2019, and has since spread globally, leading to an ongoing pandemic. Among COVID-19 patients, the percentage of patients with severe and critical COVID-19 was reported to be 13.8% and 4.7%, respectively (China CDC, 2020). The most likely cause of death was severe respiratory failure (Berlin et al., 2020). Thus, if means of respiratory support, such as non-invasive ventilation (NIV), can be chosen correctly and implemented in time, the fatality in severe patients could be reduced (Sundaram et al., 2020). However, the guidelines from different regions for NIV use in patients with COVID-19 are inconsistent.

During times of crisis, guidelines are vital for clinical practice. Evidence can be more reliable when based on well-designed guidelines. The Appraisal of Guidelines for Research and Evaluation (AGREE) II instrument is the 'gold standard' for appraising the development and quality of guidelines. On the basis of AGREE II, this review will discuss the issues that require attention when establishing guidelines during the pandemic, such as transparency in their development.

More importantly, this review will compare the clinical recommendations of each guideline from the aspects of safety issues (e.g., aerosol generation, ward selection), optimizing the interface, indications, modes, and parameter settings for NIV.

To our knowledge, this was the first review to combine the use of the AGREE II instrument for guideline development appraisal and critical assessment of the use of NIV during the COVID-19 pandemic. It is hoped that the review will address the issues that arise while developing guidelines, even in the context of a pandemic, and enhance clinicians' understanding of the use of NIV when facing COVID-19.

## Methods

This study was registered with the PROSPERO international prospective register of systematic reviews (CRD42020198410), and the results were reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statements (checklist) (Liberati et al., 2009). Further details are provided in a supplementary Word file [Additional file 1: eMethods 1].

### Guideline searches

Databases, including PubMed, Web of Science, and Cochrane Library, as well as websites of international organizations (e.g., World Health Organization and National Institutes of Health) and gray databases (e.g., Guidelines International Network and Scottish Intercollegiate Guidelines Network) were searched up to June 23,

2020. The search was limited to sources in the English language. The reference lists of eligible papers were hand-searched and experts in the field were contacted to ensure a comprehensive review. Further details are provided in a supplementary Word file [Additional file 1: eMethods 2 and eMethods 3].

### Selection of guidelines

The review included documents that focused on the management of NIV for patients with COVID-19, and only those developed by international or national health organizations or medical societies. If there were multiple versions of the document, only the latest version was included. Only documents in English were eligible, and those without a full-text version were excluded. Any papers focusing on epidemiology, nosocomial infection, quarantine, home care, prevention, clinical manifestations, or rehabilitation were excluded. Papers based on newborns, children, pregnant women, or the elderly, which could be ascertained from the title or abstract, were also excluded. Publication types such as systematic reviews, case reports, commentaries, letters, clinical trials, or handbooks were not eligible. Based on these criteria, one researcher screened the documents individually, and any uncertainty was resolved in discussion with another two researchers.

### Data extraction

The following information was extracted from each article using a standardized data extraction form: title, full issuing society name, acronym of the guideline, date of publication, country applied, region, target population, type of guideline, type of publication, development method, grading system, strength of recommendations, quality of evidence, version, developers, and number of developing organizations.

### Guideline quality assessment

Four qualified appraisers had been trained through online practice grading and pre-grading before the formal assessment. The pre-grading was carried out by randomly selecting three eligible guidelines, to ensure that each researcher had the same basic understanding of each item. The AGREE II instrument provided an objective evaluation tool for assessing the quality of guidelines. It is based on six domains and two overall guideline assessments. Each item was scored from 1 (strongly disagree) to 7 (strongly agree). Each score was derived as a percentage of the maximal possible score for each domain, using the following specific formula:

(obtained score – minimal possible score)/(maximal possible score – minimal possible score)

Double weight was assigned to the domains of rigor of development and applicability. A total score greater than 60% would be determined as 'recommended', a score between 30% and 60% as 'recommended with modification', and below 30% as 'not recommended'.

*Patient and public involvement*

No patients were involved.

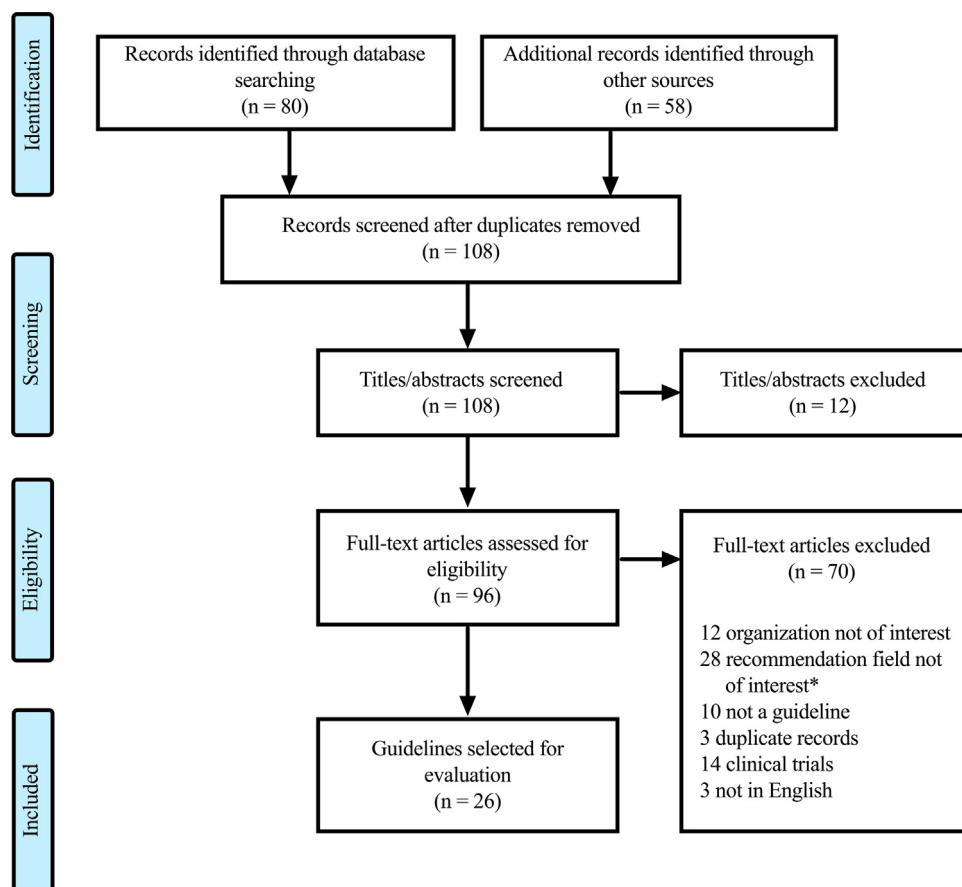
*Recommendation*

Each guideline was read in detail, with clinical recommendations related to NIV extracted, and the strength of recommendation and evidence quality recorded. The extracted content mainly included recommendations on safety issues, the optimization of NIV installation, indication for the use of NIV, the mode used, and parameter settings. The criteria for classifying the strength of recommendations and quality of evidence were different for most guidelines. To solve this problem, a new comprehensive classification criterion was applied. An additional Word file shows how the recommendations were redefined and compared [Additional file 1: eTable 1].

**Results**

*Characteristics of eligible guidelines*

A total of 26 guidelines met the inclusion criteria (Figure 1). Ten (38%) were published after April 2020. Five (WHO-toolkit, 2020; PAHO, 2020; WHO, 2020; Alhazzani et al., 2020; Thomas et al., 2020) (19%) were developed by international organizations, two (CCCGWG, 2020; NIH, 2020) (8%) were from North America, six (NCCT, 2020; ASID, 2020; NHC & SATCM, 2020; Qu et al., 2020; PCS, 2020; Indian CDC, 2020) (23%) from the Asia-Pacific region, and 13 (Sorbelli et al., 2020; ITS & IRS, 2020; Lazzeri et al., 2020; Nicastrì et al., 2020; Lombardy Section of the Italian Society of Infectious and Tropical Diseases, 2020; NHS (NIV), 2020; NHS (critical care), 2020; NHS (management), 2020; BTS, 2020; BTS (guidance), 2020; ICSI, 2020; Kluge et al., 2020; Swiss Society of Intensive Care Medicine, 2020) (50%) from Europe. Five (19%) were focused on severe or critically ill populations. Eight (31%) were self-proclaimed guidelines. Seven (27%) were developed by an evidence-based approach. Four (15%) used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system. Six (23%) provided the strength of recommendation, and four (15%) provided the quality of evidence; an additional Word file shows this in detail [Additional file 1: eTable 2]. Nine (35%) had updated versions. Seventeen (65%) were developed by a medical society, and eight (31%) were developed by more than one organization (Figure 2); an additional Word file shows this in detail [Additional file 1: eTable 3].



**Figure 1.** Flow diagram of guidelines search and selection.

\*Any papers based on epidemiology, nosocomial infection, quarantine, home care, prevention, clinical manifestations, or rehabilitation, or that were focused on newborns, children, pregnant women, or the elderly were excluded.

Quality assessment of guidelines

In AGREE II appraisal, *Scope and Purpose* (mean: 65%, range: 31–85%) and *Clarity of Presentation* (mean: 67%, range: 21–85%) had the highest average scores. *Stakeholder Involvement* (mean: 42%, range: 11–82%) and *Applicability* (mean: 39%, range: 9–67%) had the lowest average scores. *Rigor of Development* (mean: 31%, range: 5–78%) and *Editorial Independence* (mean: 28%, range: 4–88%) had the lowest average scores. As for the overall evaluation, five guidelines (19%) were recommended, sixteen (62%) were recommended with modification, and five (19%) were not recommended; an additional Word file shows this in detail [Additional file 1: eTable 4]. The overall quality as assessed by the AGREE II instrument was poor (Figure 3). The overall consistency among the four appraisers was considered good (intraclass correlation coefficient, ICC: 0.84, 95% CI: 0.81–0.86).

Recommendations

In total, 138 clinical recommendations were extracted from 26 guidelines. Only 14 (10%) provided the strength of recommendations (strong: 4, weak: 10) and six (4%) provided the quality of evidence (moderate: 3, low: 3); an additional Word file shows this in detail [Additional file 1: eTable 5]. Among the clinical recommendations, 37 (29%) were for safety issues, 20 (16%) for the optimization of NIV installation, 49 (38%) for indications for the use of NIV, and 22 (17%) for modes and parameter settings (Figure 4 and Table 1).

Discussion

During the COVID-19 pandemic, it was difficult for organizations to follow the standard procedures to design guidelines. The guidelines were based on experience gained with similar conditions to COVID-19. Failure to fully understand COVID-19 remains a great limitation, because the available research results that could be used as evidence are scarce. As for clinical practice, it is essential to gain clinical recommendations based on strictly devised guidelines in order to make accurate clinical decisions or adjust treatment plans in time.

Regarding the appraisal by using the AGREE II instrument, the guidelines' methodological quality was low, but the defects leading to the low quality were found to be resolvable. The effects of clinical recommendations would have been greatly improved, and time constraints should not have been used as an excuse because in practice this would not be a time-consuming process.

Among the six domains, *Rigour of Development* and *Editorial Independence* were of the lowest quality. Few guidelines reported the systematic methods used to search for evidence or provided the procedure for updating. Many guidelines did not record or address the funding bodies and competing interests of the development group members, which could undoubtedly affect the selection of clinical recommendations. It would not have been time-consuming to fix these defects. Without the support of systematic methods for searching evidence and providing an updated procedure, clinicians cannot take decisions confidently. Based on the limited evidence, more transparent recommendations are required, and it is essential to declare any conflicts of interest (Burls, 2010).

The quality ratings of *Stakeholder Involvement* and *Applicability* were also low. Because the development of guidelines required the

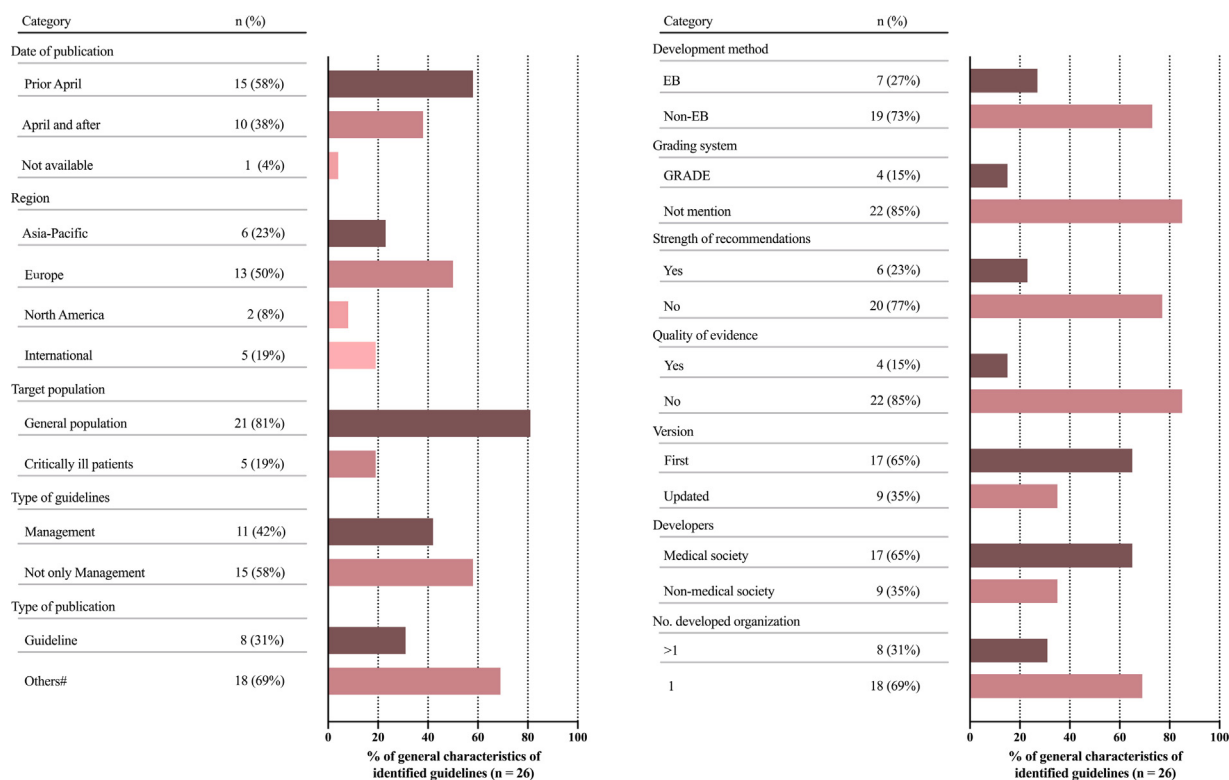
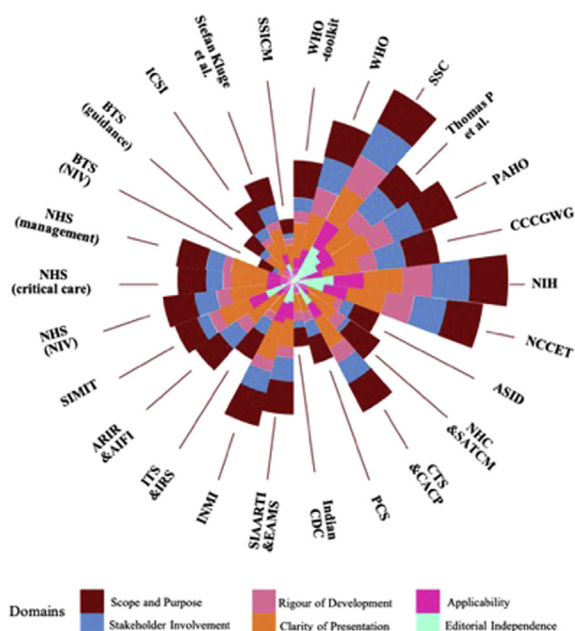


Figure 2. The general characteristics of included guidelines. n (%) means the number and its proportion among 26 guidelines. Abbreviations: EB, evidence-based; GRADE, Grading of Recommendations Assessment, Development and Evaluation. #Consensus, interim guidance, recommendations, protocol.





**Figure 3.** AGREE II domain scores for all included guidelines. The larger the area, the higher the domain score.

participation of a multidisciplinary group of experts, revealing the methodology followed was essential, but the guidelines that met this criterion were almost exclusively those developed by international organizations. Furthermore, the views and preferences of the target population were rarely sought. NIV is an essential resource; however, the regions differed in their ability to use it, which could be one reason for the variation in clinical recommendations; however, this explanation was rarely reported.

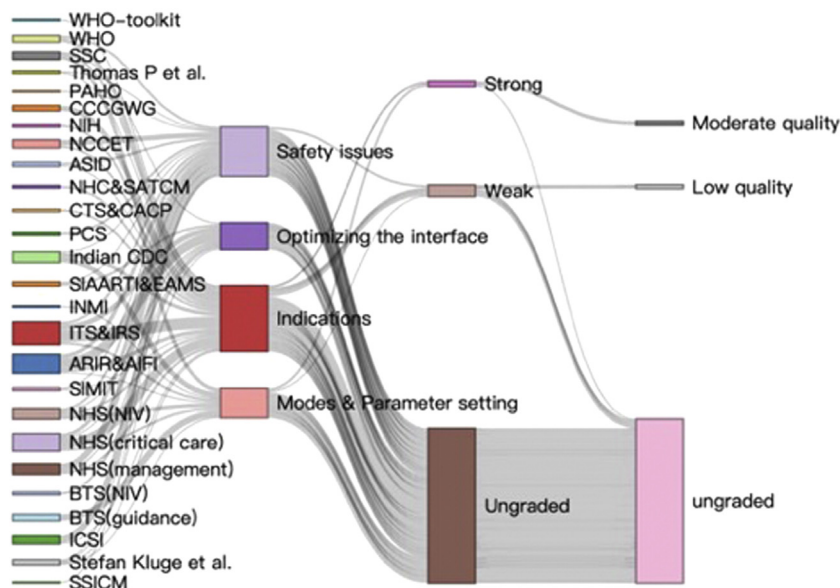
Few guidelines provided information on the strength of recommendations or quality of evidence. Even when provided, most clinical recommendations were based on previous experience of other viral pneumonia conditions and the conclusions of some observational studies, which might have been of poor quality. Using NIV as a means of respiratory support for viral pneumonia has always been controversial. When faced with

COVID-19 – a new viral disease – a clear understanding of the use of NIV was urgent.

Almost half of the guidelines provided recommendations on NIV safety issues (e.g., aerosol generation and ward selection). The clinical recommendations were relatively uniform, emphasizing that attention must be paid to aerosol generation. It has been suggested that the use of NIV would increase the risk of aerosol generation. Therefore, the guidelines suggested that NIV should be used in a single room, a negative-pressure ward, or a ward dedicated to the treatment of confirmed patients. More importantly, the medical staff should wear full personal protection equipment (eye protection, N95 or higher respirators, gloves, and long-sleeved gowns). However, NHS (management) (NHS (management), 2020) considered that NIV was mainly a droplet (>5 μm)-generating procedure rather than an aerosol (<5 μm)-generating procedure. From our perspective, this was simply based on a different definition of aerosol. Nonetheless, more attention should be paid to the increased risk of virus transmission due to patients' exhaled air.

Optimizing the interface of NIV might also reduce the risk of virus transmission. SSC (Alhazzani et al., 2020) was unable to make a recommendation regarding the use of helmet NIPPV versus mask NIPPV because of the uncertainty about its safety or efficacy during COVID-19. Three Italian guidelines (Sorbello et al., 2020; ITS & IRS, 2020; Lazzeri et al., 2020) and a German guideline (Kluge et al., 2020) suggested that helmet NIV should be the first choice among the diverse interface modes. Based on the experience in Italy, Radovanovic et al. considered the application of continuous positive airway pressure (CPAP) with the helmet, which could provide valid pulmonary support. The better tolerability of the helmet and reduced room contamination might also improve clinical management of patients, and increase the safety of the associated healthcare workers (Radovanovic et al., 2020). As mentioned in ARIR & AIFI (Lazzeri et al., 2020), using NIV with the helmet could minimize the risk of nebulization of infected material. Also, it might offer less resistance to the patient's breathing effort compared with a mask.

When helmet NIV cannot be used, Hudson and Venturi masks (Sorbello et al., 2020) or a face mask combined with a double circuit with an expiratory valve might be suggested (ITS & IRS, 2020; Lazzeri et al., 2020). If there is a need to combine a face mask with a single circuit, ARIR & AIFI (Lazzeri et al., 2020) suggested



**Figure 4.** Distribution of strength of recommendations and quality of evidence.

**Table 1**  
Recommendations for the use of NIV in COVID-19.<sup>a</sup>

Topics	Recommendation	Supporting guidelines	Number of recommendations	Strength of recommendation <sup>b</sup>	Quality of evidence <sup>b</sup>
Safety issues	Aerosol generating procedure	ICSI, PCS, Thomas et al., ITS & IRS, ARIR & AIFI, NHS (critical care), NHS (management), WHO, ASID, SIAARTI & EAMS	13	Weak: WHO	Ungraded
	Isolated environment (negative- or neutral-pressure room, switch off pressure in positive-pressure room, or cohort in restricted-access areas)	ICSI, PCS, NHS (NIV), ITS & IRS, SSCIM, NHS (critical care), NHS (management), NCCET, PAHO, SIMIT, ASID, Indian CDC	19	Ungraded	Ungraded
	Wear full PPE (eye protection, N95 or higher respirators, gloves, and long-sleeved gowns)	ARIR & AIFI, NHS (critical care), NHS (management), WHO, Kluge, et al.	5	Weak: WHO	Ungraded
Optimization of NIV installation	The use of helmet NIPPV compared with mask NIPPV	SSC, SIAARTI & EAMS, BTS (NIV), NHS (NIV), ITS & IRS, ARIR & AIFI, NHS (management), Kluge et al.	16	Ungraded	Ungraded
	An appropriate antimicrobial filter should be located	BTS (NIV), ARIR & AIFI, NHS (critical care)	4	Ungraded	Ungraded
Indications for use of NIV	Patients with worsening of respiratory status, hemodynamic instability, multiorgan failure, or abnormal mental status should not receive NIV	NHC & SATCM, SSC, CCCGWG, NHS (NIV), ITS & IRS, ARIR & AIFI, NHS (critical care), NHS (management), NCCET, WHO, CTS & CACP, NIH, SIMIT, ASID, Indian CDC	31	Weak: SSC, WHO, NIH	Low quality: SSC, NIH
	Patients with post-extubation	ICSI, Thomas, et al., NHS (critical care)	3	Ungraded	Ungraded
	Closely monitor	WHO-toolkit, NHC & SATCM, SSC, CCCGWG, NHS (NIV), ITS&IRS, ARIR & AIFI, NHS (critical care), WHO, CTS & CACP, Kluge, et al., NIH, Indian CDC	15	Strong: SSC, NIH Weak: CCCGWG, WHO	Moderate quality: NIH Ungraded
Modes and parameter settings	CPAP is indicated in hypoxemic respiratory failure, and BiPAP may be considered in certain patient groups with Type 2 respiratory failure	INMI, NHS (NIV), NHS (critical care)	5	Ungraded	Ungraded
	CPAP and FiO <sub>2</sub> value	ITS & IRS, ARIR & AIFI, NHS (critical care), BTS (guidance)	6	Ungraded	Ungraded
	SpO <sub>2</sub> should be above 90% and no higher than 96%	SSC, Kluge, et al., BTS (guidance), Indian CDC	11	Strong: SSC	Moderate quality: SSC

Other abbreviations: PPE, personal protective equipment; NIPPV, nasal intermittent positive pressure ventilation; NIV, non-invasive ventilation; CPAP, continuous positive airway pressure; BiPAP, bilevel positive airway pressure; FiO<sub>2</sub>, fraction of inspired O<sub>2</sub>; SpO<sub>2</sub>, peripheral oxygen saturation.

<sup>a</sup> The full names of the abbreviations of guidelines are shown in eTable 3.

<sup>b</sup> Strength of recommendation and quality of evidence were harmonized according to the composite grading system shown in eTable 1.

using a circuit equipped with an integrated exhalation port instead of vented masks. NIV with facemasks or hoods was the least recommended (Sorbelli et al., 2020; ITS & IRS, 2020). Moreover, an antimicrobial and antiviral filter should always be installed to limit the exhaled air's dispersion into the surrounding environment (Lazzeri et al., 2020; NHS (critical care), 2020). Guan et al. also suggested avoiding masks with vent holes and adding a filter between the mask and the vent valve to reduce viral transmission.

It has been suggested that the ward beds should be at least 1 m apart (Guan et al., 2020). Earlier randomized controlled trials indicated that NIV delivered by helmet significantly reduced the intubation rate among patients compared with patients receiving NIV by face mask. The helmet was also associated with increased ventilator-free days and significantly reduced intensive care unit (ICU) length of stay and 90-day mortality. However, a significant reduction in the intubation rate might be explained in part by the effective delivery of higher positive end-expiratory pressure (PEEP) (Patel et al., 2016). Additionally, NIV with a helmet was more comfortable for patients with acute exacerbation of chronic obstructive pulmonary disease combined with respiratory failure, and had a better effect on improving oxygenation and relieving dyspnea. Its effect on carbon dioxide emissions was no worse than that of traditional mask NIV (Liu et al., 2020). For patients with acute hypoxemia nonhypercapnic respiratory failure, excluding chronic obstructive pulmonary disease exacerbation and cardiogenic pulmonary edema, a meta-analysis by Xiu-Ping et al. showed that NIV decreased endotracheal intubation rates and hospital mortality among these patients. However, there was insufficient evidence to recommend a helmet due to the limited number of trials available (Xu et al., 2017). Helmet NIV might be beneficial during COVID-19. However, differences were shown to

exist in clinical practices across countries, regions, and hospitals because of their inherent clinical experience and supporting resources. Additionally, each measure's effectiveness was partially dependent on the indications, mode selection, and parameter settings.

Indications for NIV use were mentioned in several guidelines (WHO, 2020; CCCGWG, 2020; NCCET, 2020; Indian CDC, 2020; NHS (NIV), 2020; ICSI, 2020), which suggested that patients with worsening respiratory status, hemodynamic instability, multi-organ failure, or abnormal mental status should not receive NIV in place of other options, such as invasive ventilation or early endotracheal intubation. Such recommendations agreed with the those previously developed by the American Thoracic Society and European Society of Intensive Care Medicine (Fan et al., 2017) or the Chinese National Health Commission (NHC & SATCM, 2020). These institutions recommended that severe cases should be carefully monitored after receiving NIV. If their condition did not improve, or even worsened, within 1–2 h, then invasive ventilation and endotracheal intubation should be conducted. For using NIV in patients with post-extubation, NHS (critical care) considered there to be insufficient evidence from the UK experience to provide any guidance (NHS (critical care), 2020). However, ICSI (ICSI, 2020) suggested that NIV could be maintained in patients as long as there was no fatigue. Thomas et al. (2020) emphasized the importance of strict airborne PPE if used. To date, there has been little agreement on the use of NIV in patients with post-extubation. Previous studies have considered it to be of no benefit (Keenan et al., 2002), or even capable of causing harm because of a delay in intubation (Esteban et al., 2004). However, one study has shown that it could avoid reintubation, while reducing the length of hospital stay and mortality rate (Ferrer et al.,

2003). Considering the unknown impacts referred to above, it is deemed particularly essential to monitor the use of NIV closely, with nearly half of the guidelines providing clinical recommendations on this issue. Although some did not state the exact length of time, most guidelines recommended that patients' conditions be judged within 2 h or even 1 h after using NIV. Only NHS (critical care) suggested that the length of time could be extended to 1–4 h (NHS (critical care), 2020). To summarize, the guidelines recommended close monitoring and prompt evaluation of each patient's condition in order to prevent the use of NIV causing a delay in intubation.

Two guidelines (NHS (NIV), 2020; NHS (critical care), 2020) provided clinical recommendations for selecting NIV modes. They both considered CPAP to be indicated in hypoxemic respiratory failure, with bilevel positive airway pressure (BiPAP) possibly considered in certain patient groups with type 2 respiratory failure (e.g., chronic obstructive pulmonary disease). Pinto and Sharma held the same opinion, considering that CPAP could not be used in individuals who were not spontaneously breathing. Additionally, it was suggested that patients with poor respiratory drive needed invasive ventilation or NIV with CPAP, plus additional pressure support and a backup rate (BiPAP) (Pinto and Sharma, 2020). As for recommendations on parameter settings, NHS (critical care) suggested that low-flow CPAP was suitable for patients with a lower oxygen requirement (fraction of inspired oxygen,  $FiO_2 < 0.4$ ) (NHS (critical care), 2020). NHS (NIV) suggested that if the patient was oriented and able to tolerate a well-fitted, non-vented face mask, CPAP should be set to 10 §cmH<sub>2</sub>O, with  $FiO_2$  0.6. If further escalation was needed, CPAP could be increased to 12–15 §cmH<sub>2</sub>O, with  $FiO_2$  0.6–1.0 (NHS (NIV), 2020). ITS & IRS (ITS & IRS, 2020) and BTS (guidance) (BTS (guidance), 2020) suggested setting the CPAP value at 10–12 §cmH<sub>2</sub>O, according to the patient's needs, tolerance, and any side-effects.

Meanwhile, ITS & IRS recommended that CPAP pressures might be increased up to 15–20 §cmH<sub>2</sub>O if escalation was needed (ITS & IRS, 2020). The target value of peripheral oxygen saturation (SpO<sub>2</sub>) was different in each guideline. However, SpO<sub>2</sub> should be above 90% and no higher than 96% (Alhazzani et al., 2020; NCCET, 2020; Indian CDC, 2020; BTS (guidance), 2020; Kluge et al., 2020). The Australian guidelines suggested maintaining a value of at least 92% (NCCET, 2020). BTS (guidance) suggested that for patients with a strong respiratory drive (low or low/normal partial pressure of carbon dioxide in the arteries, PaCO<sub>2</sub>) the target should be an SpO<sub>2</sub> ≥ 94% (BTS (guidance), 2020). In patients with evidence of acute or chronic type 2 respiratory failure, SpO<sub>2</sub> should be titrated to 88–92%. Furthermore, Indian CDC suggested aiming for 92–95% and above 94% in pregnant patients and children with emergency signs, respectively (Indian CDC, 2020). Previous research by Pagano et al., which involved treating 18 patients with mild and moderate ARDS secondary to SARS-CoV-2 with non-invasive continuous positive airway pressure therapy (NI-CPAP), showed that CPAP/NIPPV could be a valid strategy for treating severely hypoxic patients, but this was only in part related to an increase in lung recruitment (Pagano et al., 2020). In the study, NI-CPAP failed in 45% of the patients, while PEEP was set to 10 §cmH<sub>2</sub>O, and  $FiO_2$  was regulated to reach a target SpO<sub>2</sub> of over 93%. It was evident that the differences in parameter settings were large across the guidelines, which might be related to the condition of the patients, operator proficiency, instrumentation, or other reasons. However, it remained difficult to form evidence-based recommendations with a lack of relevant clinical research data.

Finally, some of the included guidelines have since been updated, and some clinical recommendations on NIV have been revised as the pandemic has progressed. For instance, NCCET has deleted the statement 'In patients with hypoxemia associated with

COVID-19, do not routinely use NIV'. It now suggests that if a patient's condition worsens, then invasive ventilation and endotracheal intubation should still be used earlier (NCCET, 2020). Additionally, WHO (WHO, 2020) amended its recommendations in detail, including issues of patient selection and close monitoring.

For NIV, there remained many controversies in terms of clinical practice, including the optimization of NIV interface, indications, parameter settings, and target values for SpO<sub>2</sub>. Therefore, we combined the guidelines' development appraisals, using the AGREE II tool, and critical assessments on the use of NIV during the COVID-19 pandemic to address the issues raised while developing the guidelines, in order to reach a better understanding of the use of NIV.

Through comprehensive research, this review has provided an overview of the use of NIV. However, due to its cross-sectional nature, it should only act as a foundation for future research because some guidelines included in this review might have since been updated. Moreover, the AGREE II instrument might not be appropriate for evaluating guidelines associated with urgent conditions. Third, most guidelines were published outside bibliographic databases, and our selection process was biased towards those in the English language. Therefore, although we conducted comprehensive research, we might still have missed some relevant guidelines. Finally, recommendations for specific segments of the population are still lacking.

## Conclusion

This review emphasized the issues that should be focused on when developing guidelines for future pandemics. There is still insufficient evidence for the value of NIV. Therefore, it is vital to improve the methodological quality of the guidelines in order to make their clinical recommendations more reliable. Moreover, well-designed randomized clinical trials are needed to solve the current debate on the use of NIV.

## Author contributions

Conception and design: JXX, MJ, SYL.

Administrative support: JXX, MJ, SYL.

Provision of study materials or patients: not applicable.

Collection and assembly of data: ZFW, YZW, ZWY, HKW, JYL, HWL, HML, RCC, YEO, FYW, Yuan W, Yan W, WZL, NJL, ZTL.

Data analysis and interpretation: ZFW and YZW.

Manuscript writing: all authors.

Final approval of manuscript: all authors.

## Reporting checklist

The authors completed the PRISMA 2009 reporting checklist.

## Data sharing statement

The datasets used and/or analyzed during this study are available from the corresponding author on reasonable request.

## Conflicts of interest

All authors have completed the ICMJE uniform disclosure form. The authors have no conflicts of interest to declare.

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None.



## Ethical approval

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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## Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.ijid.2021.03.078>.

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